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Disease-a-Month

Pulmonary Failure

RICHARD V. EBERT

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received his M.D. degree from the University of Chicago. He served his internship at the Boston City Hospital and his residency at the Peter Bent Brigham Hospital. After service in the U.S. Army, he became Chief of the Medical Service at the Veterans Administration Hospital in Minneapolis and served on the faculty of the University of Minnesota. At present he is Professor and Head of the Department of Medicine at the University of Arkansas. His research interests have been in the field of cardiovascular and pulmonary physiology.

THE TRADITIONAL APPROACH to diseases of the lungs has been the study of pathology. Roentgenographic and physical findings have been correlated with the pathologic findings at operation and autopsy. The isolation of microorganisms from the sputum and the identification of tumor cells in the sputum, pleural fluid and in biopsy material have added accuracy to the diagnosis of pulmonary disease. As a result, the various pathologic entities such as pulmonary tuberculosis, bronchogenic carcinoma and bronchiectasis can be diagnosed with great accuracy.

Perhaps because of this concentration on clinical pathologic correlation, less attention has been devoted to the function of the lungs. Localized diseases of the lung, such as carcinoma, tuberculosis or lung abscess, which produce dramatic roentgenographic findings, usually have little effect on lung function. On the other hand, the generalized diseases of the lung such as pulmonary emphysema and diffuse pulmonary fibrosis may dramatically alter pulmonary function but exhibit little abnormality on roentgen examination.

The recent interest in pulmonary function is the result of the application of physiologic technics to patients with pulmonary disease. This development was largely inspired by the work of Baldwin, Cournand and Richards, who described and standardized a number of the tests of pulmonary function in common use (4). The advent of extensive surgery on the lung also stimulated interest in pulmonary function.

The function of the lung is to supply oxygen and to remove carbon dioxide from the blood. In the normal person, the lungs function so that the hemoglobin of the arterial blood is almost completely saturated with oxygen and the carbon dioxide tension of the arterial blood is maintained at a level of 40 mm. Hg. To accomplish the necessary exchange of gases, the alveoli must be ventilated with the proper quantity of air each minute. Normal ventilation is dependent on patency of the tracheobronchial tree, normal elastic properties of the lung and an intact musculature. The level of alveolar ventilation is related to the level of metabolism and is regulated mainly by the influence of the CO_2 tension and pH of arterial blood on the respiratory center.

In severe diffuse pulmonary disease there may be sufficient interference with pulmonary function to produce hypoxia or a combination of hypoxia and increase in the CO_2 tension of arterial blood. In less severe disease the blood gases may be normal and yet the patient may suffer from dyspnea. The sensation of dyspnea is related to the amount of force exerted on the lung to accomplish ventilation (29). Exertional dyspnea occurs with limitation of maximum ventilation by any disease which interferes with the mechanism of breathing. Because dyspnea is a subjective sensation, it is often difficult to evaluate. Moreover, it is affected by factors extraneous to the function of the lungs such as physical fitness and psychogenic influences. For this reason, objective means of evaluation of pulmonary function are important in the diagnosis and evaluation of pulmonary failure.

PULMONARY FUNCTION TESTS

Measurement of Lung Compartments

The simplest and most widely used test of pulmonary function is the measurement of the vital capacity. This measurement can be performed readily at the bedside with a portable bellows-type spirometer. The vital capacity should be measured in every patient complaining of dyspnea. It is more meaningful if observation of the rate of expiratory airflow is made. The vital capacity of normal people varies with sex, height and age (4).

The vital capacity can be divided into the tidal volume, the expiratory reserve volume and the inspiratory reserve volume. While these measurements may be made with a recording spirometer, the determination is of little clinical value.

The measurement of the residual volume, on the other hand, has considerable value, particularly in the diagnosis of pulmo-

nary emphysema. The residual volume is that volume of air remaining in the lungs after a maximum expiration. The usual volume in young men is between 1 and 1.5 liters, but there is considerable variation with age and body size. In one commonly used technic for measurement of the residual volume, the person inspires oxygen for 7 minutes (12). By means of a system of valves, the expired air is collected in a large spirometer. Measurement is made of the nitrogen concentration and volume of gas in the spirometer and of the nitrogen concentration of alveolar air collected at the end of the test. From this data, the amount of nitrogen and hence the volume of air in the lungs at the beginning of the breathing period can be estimated. Another method is dependent on the dilution of helium contained in a closed spirometer system by the air from the lung.

The estimation of the residual volume is not used frequently in clinical practice because facilities for these procedures are not available. For clinical purposes, a rough estimate of residual volume can be made from the roentgenogram of the lungs and the vital capacity. The total lung capacity is the amount of air contained in the lung on maximum inspiration. The residual volume can be obtained by subtracting the vital capacity from the total lung capacity. An estimate can be made of the total lung capacity from posteroanterior and lateral roentgenograms taken on full inspiration. The area of the lungs is measured with a planimeter and a formula is applied (10). A gross estimate can be made by inspection. This combined consideration of the vital capacity and roentgenogram of the chest can be helpful in the diagnosis of pulmonary emphysema. If the vital capacity is 1.5 liters and the roentgenogram reveals low diaphragms and a normal or increased area of the lungs, obviously the residual volume must be markedly increased.

Measurement of Airflow Rate

The maximum rate of movement of air from the lungs is impaired in all diseases of the lung that are accompanied by bronchial or bronchiolar obstruction. For this reason, some estimate of the rate of maximum expiratory airflow should be a part of any evaluation of pulmonary function. On the ward, this estimate can be accomplished by remarking on the rate at which the patient expires into the apparatus for measuring vital capacity. A gross but important estimate can thus be

made of rate of expiratory airflow. The measurement of vital capacity without this observation is relatively valueless. For example, the significance of a vital capacity of 2.5 liters which can be expelled in 2 seconds is vastly different from a vital capacity of 2.5 liters which is expelled in 15 seconds. If the vital capacity is measured by a technician, often no distinction is made.

A more accurate measurement of the maximum rate of expiratory airflow can be made by inspection of the spirometer tracing of expiration made with maximum effort. A spirometer with a rapidly moving drum must be used (11). Estimation of the maximum rate of expiration can also be made by the use of a timing device which permits measurement of the amount of air expelled in 1 second as well as of the total vital capacity (22). A normal person can expel 83% of his vital capacity in 1 second and can achieve a maximum expiratory flow rate of air of 8 liters per second.

Similar information can be obtained from the measurement of the maximum breathing capacity (4). In this test, the patient breathes in and out with maximum effort for 15 seconds. The volume of air moved is measured by means of a spirometer or Douglas bag. Increased resistance to expiratory airflow causes a reduction in maximum breathing capacity. Other factors such as muscular force and co-ordination, changes in the chest wall and pathologic changes in the lung influence the determination. The normal value for adult men is more than 100 liters per minute and is influenced by age and size.

Measurement of Pulmonary Mixing Index

In the normal lung, air is distributed equally to each respiratory unit. As a result, the inspired gas mixes uniformly with the alveolar air in each portion of the lung. This uniform distribution of inspired gas may not occur in diseased lungs. In pulmonary emphysema, some areas of the lung are overventilated and others are ventilated poorly. There are a number of methods of measuring abnormal distribution of inspired gas. Perhaps the simplest and most commonly used is the measurement of the nitrogen content of alveolar air after breathing oxygen for 7 minutes. This measurement can be made in conjunction with the nitrogen washout method for determining residual volume. In a normal person, the alveolar air will contain less than 2.5% nitrogen (12). Other methods such as the

continuous recording of the nitrogen content of expired air following a breath of oxygen require special apparatus.

Measurement of Blood Gases

The determination of the blood gases is an important method of evaluating the function of the lungs. The measurement of oxygen saturation must be done on arterial blood. The removal of a sample of blood from the femoral or brachial artery is a simple procedure and is essentially without hazard. The blood is collected in a lightly oiled syringe. Air bubbles should be avoided. A small amount of liquid heparin in the syringe is used as an anticoagulant and also to displace the air. After drawing the blood, a few drops of mercury are drawn into the syringe to aid in mixing the blood. The syringe is capped with an occluded needle and placed in ice water. The blood can be introduced directly into the pipette. The oxygen content of the blood is measured with the manometric Van Slyke apparatus. The oxygen capacity is measured after equilibration of the blood with room air in a tonometer or in the chamber of the Van Slyke apparatus.

Because of the shape of the oxygen dissociation curve of blood, the oxygen saturation does not become appreciably lowered until the oxygen tension is decreased by 30 mm. Hg. Thus, the direct determination of oxygen tension is a more delicate index of pulmonary function. Unfortunately, this determination is technically difficult.

In pulmonary disease, there is often an increase or decrease in the carbon dioxide tension of the arterial blood as a consequence of overventilation or underventilation of the alveoli. Carbon dioxide tension is the partial pressure of CO_2 in a bubble of gas which is in equilibrium with the gas in the blood. The CO_2 in the blood is chiefly in the form of carbonic acid. The carbonic acid together with the bicarbonate of the blood forms an important buffer system. Increase in CO_2 tension and carbonic acid leads to a decrease in blood pH and an increase in bicarbonate as a result of shifts in the other buffer systems. Thus, the pH and bicarbonate content of the blood are dependent on the CO_2 tension (38).

The CO_2 tension may be determined directly by equilibration with a bubble of gas. More commonly it is calculated from a nomogram after determining the CO_2 content and pH of the blood (38). If this determination is not possible, information

of value may be obtained from the determination of the CO_2 content of blood. This determination is usually done on venous blood withdrawn in the usual manner. The plasma is separated from the cells and equilibrated with normal alveolar air or with gas containing an equivalent amount of CO_2. The CO_2 content of the plasma is then determined. It is evident that the CO_2 content determined in this manner is not the same as the CO_2 content of the blood as it circulates through the arteries of the patient. The determination does measure the bicarbonate of the plasma under the specified conditions. Hence, valuable information regarding the plasma buffering system is obtained. In chronic pulmonary disease with increase in CO_2 tension there is a decrease in chloride content of the plasma and an increase in bicarbonate. This result is related to renal excretion of chloride and retention of bicarbonate, and serves to maintain the plasma pH at a relatively normal level. This alteration in the anions of the plasma results in an increase in the ability of the plasma to bind CO_2. Thus, the determination of the plasma CO_2 combining power is helpful in the detection of chronic elevation of CO_2 tension. Caution must be exercised in interpretation, since a similar change in the plasma anions may occur with the hypochloremic metabolic alkalosis which accompanies the administration of mercurial diuretics. A differentiation can be made only by determination of the blood pH.

A more refined method of studying gas exchange in the lungs has been developed by Riley (34, 35). This is dependent on the concept of ideal alveolar air. Despite the wide divergence in gas exchange which may occur in separate alveoli, the total gas exchange must be such that the same amount of CO_2 is added to the alveolar air per minute as is extracted from venous blood. Conversely, the same amount of oxygen must be added to venous blood per minute as is extracted from alveolar air. This is equivalent to stating that the respiratory quotient (RQ) of the gas exchanged from the blood is the same as the RQ of gas exchanged from the alveoli. Knowing this RQ and the CO_2 tension and O_2 tension of venous blood together with the appropriate oxygen and carbon dioxide dissociation curves, it is possible to plot a curve which represents the possible values for CO_2 tension and O_2 tension which can be found in mixed blood leaving the alveolar capillaries. If the lung is now considered as a uniformly ventilated and perfused organ, the values for CO_2 tension and O_2 tension in alveolar air which are possible for a given RQ can be plotted. The intersection of these two

lines gives the O_2 tension and CO_2 tension of ideal alveolar air.

The composition of expired air can be considered the result of the admixture of inspired air with ideal alveolar air. The composition of arterial blood can be considered to be the result of the admixture of blood with an O_2 tension and CO_2 tension identical with ideal alveolar air and mixed venous blood. In this manner, the dead space and venous admixture values are calculated. There is a wide variation in ventilation perfusion relationships and in gas exchange in the various alveoli of the lung in emphysema. Some areas of the lung are well ventilated and poorly perfused while others are poorly ventilated and well perfused. The former areas will contribute to the dead space admixture and the latter to the venous admixture.

It is apparent from this brief discussion of the studies of Riley that his concepts involve an abstract formulation of the problems of gas exchange in the lung. Moreover, difficult technical studies are involved. While the work has contributed greatly to an understanding of gas exchange in the diseased lung, the methods are not suitable for routine clinical use.

Studies of the difference in oxygen tension between alveolar air and arterial blood have been used to determine the relative importance of venous admixture and impaired diffusion of gas across the alveolar membrane in the production of hypoxia (34). Breathing air of low oxygen concentration increases the effect of impaired diffusion, whereas breathing air of high oxygen concentration eliminates the effect of impaired diffusion. True shunts between the pulmonary artery and pulmonary veins together with perfusion of nonventilated lung can be measured by having the patient breathe pure oxygen and measuring the difference in O_2 tension between alveolar air and arterial blood (7). The determination is not influenced significantly by impaired diffusion of oxygen across the alveolar membrane or by alveoli with a low ventilation perfusion ratio.

Recently, there has been considerable interest in the diffusion capacity for carbon monoxide. Diffusion capacity is the amount of a given gas which diffuses into the blood per minute divided by the pressure gradient in mm. Hg between the alveolar gas and alveolar capillary blood. The gradient of pressure is the mean gradient over the entire length of the capillary, not the gradient of the end of the capillary. The diffusion capacity for oxygen can be estimated by the Riley method if the studies are made at two levels of oxygen concentration in the inspired air. Carbon monoxide is extremely useful in the measurement

of diffusion capacity because of its great affinity for hemoglobin (17). As a result of this combination with hemoglobin, the tension of CO in the blood is almost zero. Hence, the gradient of CO between alveolar air and capillary blood can be determined by measuring the concentration of CO in alveolar air. The diffusion capacity is influenced not only by the nature of the membrane between the alveolar air and blood but also by the total surface over which diffusion occurs.

DISEASES LEADING TO PULMONARY FAILURE

Airway Obstruction

Airway obstruction occurs occasionally from lesions of the larynx or pressure on the trachea. Bronchial asthma is a more common cause. A fortunate feature of bronchial asthma is the intermittent nature of the symptoms. During an attack, the person may be desperately striving to breathe and suffering from hypoxia, but relief eventually comes either spontaneously or with the help of drugs.

Bronchial asthma is often confused with pulmonary emphysema. The distinction is made more difficult by the fact that long-standing bronchial asthma is frequently complicated by pulmonary emphysema. The differentiation of the two diseases is of considerable importance from the standpoint of both prognosis and therapy. Pulmonary function tests are of no aid in making this distinction during an acute episode of bronchiolar obstruction. If a complete remission of bronchial asthma can be produced, pulmonary function tests can be used to determine the degree of complicating emphysema. It may be necessary to use cortisone to produce such a remission. A patient with bronchial asthma without complicating emphysema should have normal pulmonary function tests for his age if a remission of the bronchiolar obstruction can be produced.

Pulmonary Emphysema

Pulmonary emphysema is by far the commonest cause of chronic pulmonary failure. It may occur without evident predisposing diseases or it may complicate bronchial asthma, bronchiectasis or silicosis. Pulmonary emphysema should always be suspected when pulmonary insufficiency is present.

The history of a patient with pulmonary emphysema is usu-

ally characteristic. The patient first notices a slight limitation of activity as a result of exertional dyspnea. He also complains of a chronic cough. In time, he finds that he can tolerate less and less exertion. He also notices a marked exacerbation of his dyspnea associated with acute respiratory infections. Finally, he becomes almost completely incapacitated and has dyspnea on the slightest exertion. He may now note dyspnea at rest and he finds that he sleeps more comfortably in the sitting position. Cyanosis may be present and edema of the legs may appear. At this stage an acute respiratory infection may be followed by intolerable dyspnea, severe cyanosis and evidence of right heart failure.

The physical examination is less characteristic of pulmonary emphysema than the patient's history. The presence of visible cyanosis is variable. Many patients with emphysema have a normal or only slightly decreased oxygen saturation of the arterial blood. Cyanosis will not be present in these patients. The less common patient with severe hypoxia, polycythemia and right heart failure may show intense cyanosis. The term black cardiac has been used to describe these patients.

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well outside the midclavicular line in emphysema. This test is helpful in differentiating this disease from left ventricular failure. The absence of murmurs and the relative infrequency of auricular fibrillation in emphysema also help in diagnosis.

Evidence of right heart failure may be present in advanced pulmonary emphysema. The most useful sign is distention of the neck veins or elevation in the measured venous pressure. Hepatomegaly and edema may also be present in right heart failure. Some care must be exercised in evaluating both these findings. The liver may be palpable in uncomplicated pulmonary emphysema because of the low diaphragms and flaring costal margins. Edema of the lower legs may result from prolonged dependency of the extremities.

The radiologic findings in pulmonary emphysema are variable and often not of diagnostic value. It is always shocking to observe a relatively normal chest roentgenogram of a patient who is dying of pulmonary emphysema. The lack of relationship between the severity of the clinical disease and roentgenographic findings has been documented in a British study (28). The reason for the lack of correlation is that the bullae, the basic pathologic lesion, are often not visible in the roentgenogram. The degree of fibrosis associated with emphysema is variable. The finding of flattened diaphragms is helpful in diagnosis. Inspiration and expiration films or fluoroscopy are useful in visualizing the motion of the diaphragms. As mentioned earlier, the roentgenograms are more meaningful if interpreted with a knowledge of the vital capacity. This knowledge enables one to estimate the residual volume, which is always increased in emphysema.

Most of the recent advances in the diagnosis of pulmonary emphysema are the result of studies of the pathologic physiology of the lungs. The changes in physiologic measurements are usually marked and characteristic even though the roentgenographic findings may not be striking (39).

One of the consistent findings in emphysema is a change in the lung compartments. The residual volume is increased, the vital capacity decreased and the total lung capacity is normal or increased. In simple terms, the lungs do not collapse in a normal manner and consequently contain much more air at the end of a maximum expiration than normally. This failure to collapse is related to a change in the elastic properties of the lungs (21). The elasticity of the lungs is necessary for normal function. The lung can be compared with a rubber balloon

which requires pressure to inflate it. The greater the pressure the greater the volume of the balloon. The effective pressure is the difference in the pressure within the balloon and the pressure outside the balloon. The elastic properties of the

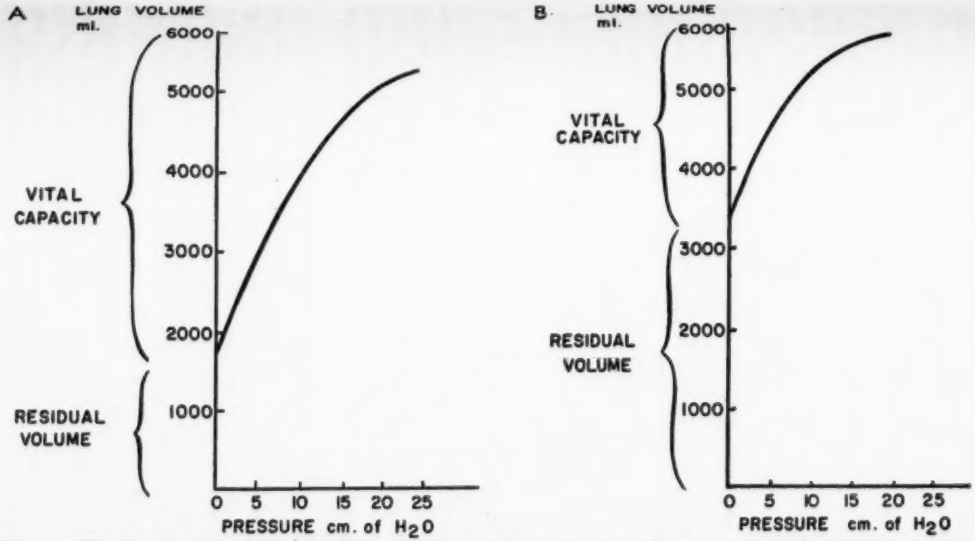

FIG. 1.—The lung compartments and the pressure volume curve of the lungs in a normal human being, *A*, and a patient with pulmonary emphysema, *B*. Note that in the patient with emphysema the lung is inflated to much greater volume by a given pressure than in the normal subject. (From Ebert, R. V., The clinical significance of the elastic properties of the lung, Ann. Int. Med. 45:589, 1956.)

which requires pressure to inflate it. The greater the pressure the greater the volume of the balloon. The effective pressure is the difference in the pressure within the balloon and the pressure outside the balloon. The elastic properties of the balloon can be described by the relationship between pressure and volume. In the instance of the lung, the significant pressure is the static intrathoracic pressure which is negative, while the pressure within the lung is atmospheric under static conditions with the glottis open. The intrathoracic pressure can be estimated by measuring either intrapleural pressure or intraesophageal pressure. A pressure volume diagram can be constructed by measuring intrathoracic pressure and volume at various degrees of inflation of the lungs (Fig. 1, *A* and *B*). Less pressure is required to inflate the lung in emphysema to a given volume than to inflate the normal lung. The emphysematous lung is like an overstretched balloon. As the residual volume is approached, the pressure reaches zero and hence the lung fails to collapse further. Thus, the marked increase in residual volume in emphysema is a reflection of the altered elasticity of the lung.

Another important physiologic finding in emphysema is an increase in resistance to flow of air (21, 30). It is generally agreed that the increase in resistance occurs in the smaller air passages but the cause is not entirely clear. It may be related in part to unequal rates of flow in various bronchioles, in part to turbulence of air associated with bullae and in part to actual narrowing of bronchioles. In any case, bronchial infection, a common complication of emphysema, greatly increases the airway resistance.

Patients with emphysema characteristically have a greatly reduced rate of airflow during expiration. Inspiration can be accomplished with much less difficulty. The reduced rate of airflow is seen particularly at the end of a forced expiration when the patient seems to squeeze air out at a slow rate. This marked reduction in the rate of expiratory airflow is related both to the increase in airway resistance and to the alteration in the elastic properties of the lung. Studies relating rate of airflow to intrathoracic pressure have shown that applying positive pressure to the lung causes little increase in rate of airflow because the positive pressure in the thoracic cavity tends to collapse the smaller air passages. Thus, maximum airflow occurs when the intrathoracic pressure is atmospheric and the lung is collapsing without external pressure. Under

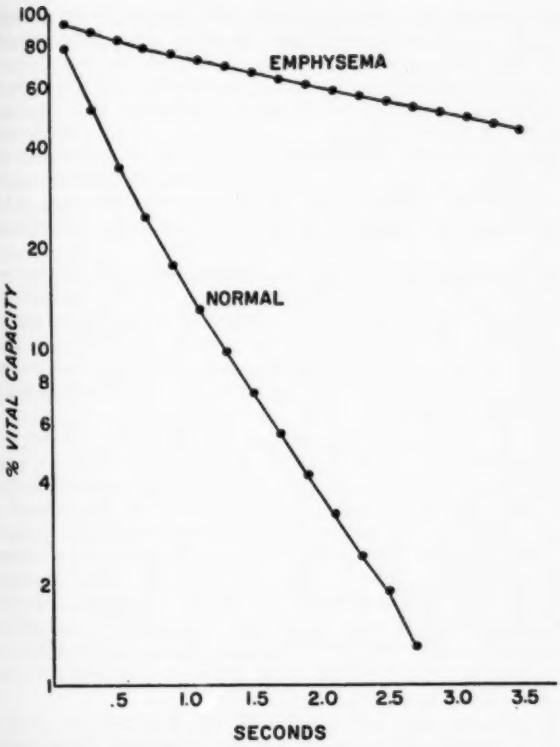

FIG. 2.—The maximum rate of expiratory airflow in a normal human being and a patient with pulmonary emphysema. Note that at 1.0 second the patient with emphysema has expelled only 27% of his vital capacity whereas the normal subject has expelled 85% of his vital capacity.

these circumstances, the rate of movement of air from the lung will be dependent on the elastic pressure in the lung or pressure volume diagram and on the resistance to airflow. A simple analogy is a rubber balloon with a narrow opening. The rate of collapse of the balloon will be related to its elastic properties and to the resistance to movement of air at the outlet.

The alteration of the maximum rate of expiratory airflow in emphysema can be demonstrated in many ways. The reduction in maximum breathing capacity is related to this defect in pulmonary ventilation. The reduction in the ratio of 1 second to total vital capacity is similarly related to this change in expiratory airflow. The abnormality can also be demonstrated by simply having the patient expire into a spirometer at a maximal rate of speed. It is for this reason that vital capacity is of maximal value in the diagnosis of emphysema only if accompanied by some estimation of the rate of expiratory airflow.

Another physiologic defect in emphysema is interference with the normal distribution of inspired gas. In the normal lung, the elasticity and resistance to airflow in each unit of the lung is approximately the same. Consequently, inspired gas is distributed evenly. In emphysema, there are marked regional differences in resistance and compliance and the inspired gas is distributed unevenly.

The change in blood gases also appears to be related to regional differences in ventilation. The total resting ventilation in liters per minute is normal or slightly increased in patients with emphysema. Despite this fact, some of the alveoli are poorly ventilated, as evidenced by the elevated CO_2 tension in the arterial blood. The explanation for the discrepancy between total ventilation and effective alveolar ventilation appears to be in the relationship between perfusion and ventilation. Some areas of the lung are well ventilated but poorly perfused with blood. Such areas might be avascular bullae where little or no gas exchange occurs. Other areas are well perfused with blood but are poorly ventilated.

All patients with emphysema do not demonstrate alteration in blood gases while at rest or during exercise. Those patients with normal blood gases may complain of marked dyspnea. Curiously enough, there are patients with rather marked alterations in blood gases who have no complaint of severe dyspnea.

The characteristic change in emphysema is a decrease in the oxygen saturation of the arterial blood and an increase in CO_2 tension. In the usual patient, the blood pH will be normal or only slightly decreased because of a compensatory increase in plasma bicarbonate. In association with an acute respiratory infection or interference with ventilation from some other cause, the CO_2 tension may rise abruptly. The pH then falls.

Coma often occurs and, as a consequence, death may ensue.

The ventilatory response to CO_2 is impaired in patients with emphysema (1). If the concentration of CO_2 in the inspired air is increased, the patient with emphysema will increase his ventilation less than will the normal person despite a rise in blood CO_2 tension. This apparent insensitivity of the respiratory center to CO_2 may be related in part to the increase in plasma bicarbonate. On the other hand, hypoxia serves as an effective stimulus to ventilation. The effectiveness of the hypoxic stimulus and the ineffectiveness of the CO_2 stimulus can be demonstrated readily by administrating oxygen to a patient with emphysema. The arterial oxygen saturation rises to 100%, the P_{CO_2} rises and the level of ventilation falls. This phenomenon has important implications as to oxygen therapy and will be discussed later.

The occurrence of polycythemia in association with hypoxia in pulmonary emphysema is extremely variable. Polycythemia and increase in hemoglobin content of the blood is a compensatory phenomenon in patients with hypoxia. It is seen regularly in people living at high altitudes and is considered to be an important adaptive mechanism. It is also seen regularly in patients with congenital heart disease, but is frequently absent in patients with emphysema and hypoxia. The reason for this is not entirely clear but may be related to the repeated infections which plague these patients. On the other hand, occasional patients with emphysema will demonstrate marked polycythemia. These patients often have cor pulmonale and right heart failure.

The Senile Lung

It is well known that as a person grows older, the lung's vital capacity diminishes. With this diminution in vital capacity there is often an increase in residual volume (32). Changes also occur in the elastic properties of the lung and in the distribution of inspired gas. All these changes are similar to those which occur in pulmonary emphysema. There is, however, no increase in the resistance to airflow, and the blood gases are normal.

While these changes in pulmonary function ordinarily do not lead to symptoms, apparently they may render the elderly person more vulnerable to the effects of bronchitis or bronchial obstruction.

Pulmonary Fibrosis

Localized pulmonary fibrosis has little effect on pulmonary function. If the fibrosis is extensive and bilateral, there may be marked alteration in pulmonary function. This type of fibrosis may be seen in advanced bronchiectasis, pulmonary tuberculosis and silicosis. It is often complicated by pulmonary emphysema. The general clinical picture does not differ greatly from that seen in emphysema except that the total lung capacity is often reduced.

A rather distinctive clinical picture may occur in association with diffuse pulmonary fibrosis occurring in berylliosis, sarcoidosis, Hamman-Rich syndrome, scleroderma with pulmonary involvement, radiation fibrosis, miliary tuberculosis and fungous infections of the lungs. On roentgenographic examination, the lungs exhibit a fine miliary or reticular type of lesion which involves both lungs diffusely. On microscopic examination of the lung, thickening of the alveolar septa with interstitial fibrosis is observed.

From the physiologic standpoint, these patients differ sharply from patients with pulmonary emphysema (3, 5, 42). The vital capacity and total lung capacity may be normal or reduced to a variable degree. In contrast to emphysema, the residual volume is not increased. Characteristically, there is no interference with expiratory airflow. As a consequence, the maximum breathing capacity remains normal or is only slightly reduced. In the milder forms of the disease, the arterial oxygen saturation may be normal at rest and during exercise. The arterial CO_2 tension is often lowered because these patients exhibit hyperventilation during both rest and exercise. The mechanism of this hyperventilation is not clear but the stimulus presumably is neurogenic and originates in the lungs.

In the more advanced forms of the disease there is a decrease in the oxygen saturation of the arterial blood. Although it may be present at rest, this condition is often greatly accentuated by exercise. The CO_2 tension remains normal or is even decreased because the alveoli are adequately ventilated or overventilated. The thickened alveolar walls lead to a marked increase in the gradient of oxygen between alveolar air and pulmonary capillary blood. Moreover, some of the blood passes through the lung without any exchange of oxygen occurring. Because CO_2 diffuses much more readily than does O_2 and because the alveoli are overventilated, there is no increase in the tension of CO_2 in arterial blood. The characteristic dis-

turbance in diffusion of O_2 has led to the term alveolar capillary block.

The characteristic symptom of this disorder is dyspnea. In the disease's late stages cyanosis and cor pulmonale may be present. Diagnosis may be difficult in the milder form of the disease. The patient may be dyspneic but exhibit few findings on routine pulmonary function studies. Careful roentgenologic studies and even pulmonary biopsy may be necessary to elucidate the mechanism of the dyspnea. At times, these patients may be falsely diagnosed as anxiety neurosis with hyperventilation. It should also be emphasized that this syndrome occurs in association with a variety of disease states and that every effort should be made to establish an etiologic basis for the pathologic changes in the lungs.

Marked Chest Deformity

Deformities of the chest which lead to limitation of the vital capacity are kyphosis, scoliosis, pectus excavatum or funnel chest and rheumatoid arthritis of the spine. Pulmonary failure usually occurs in those patients with severe kyphoscoliosis and marked distortion of the thoracic cavity.

The chief symptom in these patients is dyspnea which may become progressively more severe, causing death at an early age. A group of these patients were carefully studied by Chapman, Dill and Graybiel (9). A marked reduction in vital capacity was observed. The total lung capacity was reduced in most of the patients and the ratio of residual volume to total lung capacity was increased. The oxygen saturation of the hemoglobin of the arterial blood was decreased in one patient and normal in the rest. Apparently, in those patients with marked reduction in vital capacity the occurrence of respiratory infection with bronchitis or pneumonia leads to severe pulmonary failure and often death.

Pleural Thickening

Pleural adhesions or minor fibrous thickening of the pleura may have no effect on pulmonary function. Massive thickening of the pleura which sometimes follows empyema, tuberculous pleuritis or prolonged artificial pneumothorax may lead to severe impairment of function of the involved lung. The lung

is usually atelectatic and the mediastinum displaced to the affected side.

If the disease is unilateral, the function of the lung can best be studied by bronchospirometry (23). In this way, the ventilation and oxygen uptake of the two lungs can be compared. In severe pleural disease not only may ventilation of the involved lung be diminished but also the oxygen uptake of this lung may be reduced markedly.

Fortunately, pleural thickening is usually unilateral. If the opposite lung is functioning normally little disability results. The oxygen saturation of the arterial blood is not appreciably lowered because the blood flow is diminished through the diseased lung. In severe pleural involvement with almost total loss of function of one lung, the result is comparable to a pneumonectomy. Occasionally, an odd chain of events occurs. Pleuritis with atelectasis and loss of function of one lung develops. The mediastinum shifts to this side with an apparent increase in volume of the opposite lung. The lung without pleural involvement appears normal radiographically but progressive loss of pulmonary function occurs with eventual death from pulmonary failure. Presumably, the uninvolved lung was emphysematous but symptoms did not ensue until the function of the involved lung was destroyed by pleuritis. The role of overdistention of the lung is not clear. A similar event sometimes occurs after pneumonectomy.

Pulmonary Failure in Obesity

In the past few years there have been a number of reports of patients with marked obesity who exhibit a syndrome characterized by hypoxia, polycythemia and pulmonary hypertension (2, 8). Not all patients with marked obesity have this syndrome, but those who do commonly complain of marked somnolence. They may also have Cheyne-Stokes respiration at times, and evidence of right ventricular failure may be present.

Physiologic studies on these patients reveal a reduction in vital capacity with a marked reduction in expiratory reserve volume. The functional residual volume is also markedly reduced. While the maximum breathing capacity is reduced to a variable degree, there is no evidence of obstruction to expiratory airflow. The tidal volume is decreased and the frequency of breathing increased. The oxygen saturation of the hemoglobin of the arterial blood is often markedly reduced. The

CO_2 tension of the arterial blood is elevated to a variable degree. The pulmonary arterial pressure is elevated and the cardiac output is normal or increased.

The mechanism of production of this syndrome is not entirely clear. It is apparent that the response of ventilation to chemical stimuli is inadequate. Alveolar hypoventilation is present despite an elevated CO_2 tension and hypoxia. Apparently, the work of breathing is increased by the marked obesity and the mechanism of breathing may be altered by the decrease in functional residual volume. Whether the marked somnolence and decrease in the response of ventilation to chemical stimuli are the result of prolonged CO_2 retention is not entirely clear. The theory that obesity plays a primary role is supported by the fact that these patients may improve with weight reduction. The hypoxia is related both to decrease in alveolar ventilation and perfusion of nonventilated alveoli.

Interestingly, almost all these patients exhibit polycythemia, the finding of which often calls attention to the syndrome. This is in contrast to patients with pulmonary emphysema where the hematologic response to hypoxia is quite variable. The pulmonary hypertension is also of interest as these patients have no primary disease of the lungs. It appears to be related to hypoxia, polycythemia and atelectasis with increased resistance to blood flow.

This syndrome, which seems to be reasonably common, should be searched for in all extremely obese patients. We have recently seen a patient who superficially appeared to fit this syndrome, but more careful studies revealed an increase in residual volume and an abnormality in intrapulmonary mixing of inspired gas. Most likely this patient had a combination of emphysema and marked obesity (27).

The somnolence in some of these patients has been more than might be expected on the basis of the change in blood gases. One wonders whether the somnolence, obesity and failure of the respiratory center to respond normally may all be related to an unknown factor.

Paralysis of Respiration Muscles

Paralysis of respiration muscles, from whatever cause, leads to a reduction in vital capacity. If the paralysis is severe, there will be alveolar hypoventilation with decrease in oxygen saturation and increase in the CO_2 tension of arterial blood.

COR PULMONALE

Right ventricular hypertrophy is observed commonly at autopsy in patients with pulmonary emphysema or pulmonary fibrosis. These patients may exhibit the signs of right ventricular failure before death. The development of cardiac catheterization has permitted study of the pulmonary circulation and has elucidated the mechanisms involved in cor pulmonale.

Before discussing the changes in the pulmonary circulation in diseases of the lungs it is advantageous to review the physiology of the normal pulmonary vascular system. The pulmonary arterial pressure is low, the mean pressure being approximately 15 mm. Hg. There is only a small gradient of pressure between the pulmonary artery and pulmonary veins. The pulmonary artery pressure does not increase with an increase in pulmonary blood flow up to 2½-3 times the resting flow. The pulmonary capillary pressure is well below the colloid osmotic pressure of the plasma. Consequently, the normal person is protected against the development of pulmonary edema.

Pulmonary hypertension can be produced by two mechanisms. In the first instance there is an increase in pulmonary blood volume with consequent distention of the pulmonary vascular system. The pressure is increased in the pulmonary veins, pulmonary capillaries and pulmonary artery. Pulmonary edema occurs if the elevation in pressure is marked. The gradient of pressure from artery to capillary to veins is not changed greatly. This type of pulmonary hypertension occurs in left ventricular failure, and with the sudden intravenous administration of large amounts of fluid. In the second type of pulmonary hypertension the pulmonary arterial pressure is elevated but the pulmonary capillary and pulmonary venous pressures are normal. The resistance to flow is increased in the small arteries. Pulmonary edema does not occur. This type of hypertension occurs in association with pulmonary disease and is also observed in certain types of congenital heart disease and in so-called primary pulmonary hypertension. Finally, in certain instances of heart disease such as mitral stenosis, both mechanisms may operate to produce pulmonary hypertension.

Recently, extensive studies of the pulmonary arterial pressure have been made, especially by Harvey and his colleagues (25). The pulmonary arterial pressure is elevated to a variable degree in pulmonary emphysema. In those patients without hypoxia the elevation in pressure is usually slight or the pres-

sure may be normal when the patient is resting. The elevation is the greatest in those patients with hypoxia and right ventricular failure. There is considerable correlation between the degree of hypoxia and the elevation in pulmonary arterial pressure. On the other hand, there is a poor correlation between the ratio of residual volume to total lung capacity and the pulmonary arterial pressure.

The mechanism of production of pulmonary hypertension in emphysema is complex. The decrease in size of the vascular bed as a result of destruction of lung parenchyma undoubtedly plays an important role. Hypoxia also appears to be important. The correlation between pulmonary hypertension and hypoxia has already been mentioned. Hypoxia in the normal person can produce some increase in pulmonary arterial pressure. Moreover, relief of hypoxia in emphysema may lead to a lowering of pulmonary arterial pressure. When polycythemia is marked, the increased viscosity of the blood may increase the resistance to blood flow.

In other types of pulmonary disease similar mechanisms are at play and produce pulmonary hypertension. In pulmonary fibrosis, the destruction of the pulmonary vascular bed is probably of great importance. In the pulmonary hypertension of the obesity syndrome, hypoxia and polycythemia are important in increasing pulmonary vascular resistance.

The cardiac output in patients with pulmonary emphysema is somewhat variable (19). It may be normal, increased or decreased. The correlation of cardiac output and degree of hypoxia is rather poor. In patients with right ventricular failure, the output is usually normal or even increased. This condition distinguishes the failure of cor pulmonale from the more usual forms of heart failure in which the cardiac output is uniformly decreased.

Right ventricular failure in emphysema is commonly precipitated by an episode of bronchial infection with an acute exacerbation of hypoxia. This episode in turn increases the pulmonary hypertension. It seems likely that the hypoxia also has a deleterious effect on myocardial function. The signs of right ventricular failure are the usual ones: elevated venous pressure, enlarged liver and edema. The most reliable sign of right ventricular failure is a distinct rise in venous pressure.

Dilatation of the right heart may be difficult to evaluate in the roentgenogram because of the vertical position of the heart and the changes in the lungs. The enlargement of the heart is

best visualized in serial roentgenograms. If the roentgenograms during failure are compared with those taken before and after the episode, a distinct difference in heart size will be observed. An extreme degree of cardiac enlargement is unusual.

The best criterion of right ventricular hypertrophy would appear to be the electrocardiogram. Johnson and co-workers (26) studied 40 patients with chronic pulmonary disease and compared the electrocardiographic findings with the pulmonary artery pressure. They found that all the patients with a typical pattern of right ventricular hypertrophy, except one, had a pulmonary artery pressure of 30 mm. Hg or greater. They also noted a high incidence of rsR^1 pattern in the right-sided precordial leads in patients with chronic pulmonary disease. This pattern which is sometimes termed incomplete right bundle branch block was also correlated with a high level of pulmonary artery pressure. They noted that a number of patients with mild or moderate pulmonary hypertension showed no characteristic electrocardiographic changes.

Of great importance is the clinical significance of right heart failure. There is a tendency to regard right ventricular failure as an important factor in fatal chronic pulmonary disease. This seems incorrect from an analysis of our present knowledge. Death appears to result from hypoxia or respiratory acidosis which are a result of alterations in pulmonary function. There is no reason to believe that the right heart failure in chronic pulmonary disease alters pulmonary function. Harvey (25) has pointed out that if left heart failure played a role in the terminal phase of chronic pulmonary disease, one would expect a decline in pulmonary artery pressure with the administration of digitalis. This decline does not occur. Moreover, Dexter (13) has found that the pulmonary capillary pressure is not elevated in severe pulmonary emphysema. A marked reduction in cardiac output does not occur and hence the blood flow to the various organs must be reasonably adequate. Apparently, right heart failure is of great importance because it calls attention to the severity of the pulmonary failure. Therapy should be directed primarily toward the lung disease and toward relieving the hypoxia and respiratory acidosis.

RECOGNITION OF PULMONARY FAILURE

The possibility of pulmonary disease should be considered whenever a patient complains of dyspnea. One common prob-

lem is the question of whether dyspnea is psychogenic in origin, related to pulmonary disease or whether both factors are involved. Since dyspnea is a subjective sensation, it cannot be measured. Patients with an anxiety neurosis often hyperventilate or have abnormal patterns of breathing and commonly complain of dyspnea. Emotional factors also are important in the degree of dyspnea experienced by patients with pulmonary disease. An evaluation of the role played by pulmonary disease in the production of dyspnea can usually be made by a careful history, physical examination, roentgenographic examination and simple studies of pulmonary function.

Another common problem is the distinction between dyspnea associated with pulmonary congestion and edema consequent to heart failure and dyspnea related to primary disease of the lungs. This differentiation may be made more difficult when right ventricular failure accompanies pulmonary disease. If certain general principles are followed, errors in differential diagnosis seldom will be made. Left ventricular failure is invariably accompanied by enlargement of the heart, specifically of the left ventricle. Often the apex impulse can be felt well outside the left midclavicular line. The roentgenogram will usually give evidence of left ventricular enlargement. The electrocardiogram may show left ventricular hypertrophy. The circulation time is prolonged. On the other hand, in pulmonary failure the heart may be normal in size or may give evidence of enlargement of the right ventricle. The apex impulse is not ordinarily felt outside the left midclavicular line. Significant murmurs are uncommon. The ECG may be normal, it may reflect change in position of the heart or it may give evidence of right ventricular hypertrophy. The circulation time is normal or only slightly prolonged. Auricular fibrillation is relatively uncommon.

Major difficulty in diagnosis is most likely to be encountered in diseases of the heart producing chiefly right ventricular hypertrophy. In mitral stenosis the murmur and evidence of left atrial enlargement usually serve to make the differentiation. Occurrences of primary pulmonary hypertension and congenital heart disease occasionally may be confused with those of pulmonary failure.

Studies of pulmonary function are helpful in the differentiation of pulmonary disease from primary disease of the heart. In left ventricular failure or mitral stenosis the vital capacity and the total lung capacity are diminished and the residual

volume is normal. The rate of expiratory airflow usually is not impaired, although in the presence of pulmonary edema there is some increased resistance to airflow. The oxygen saturation of the hemoglobin of the arterial blood is not usually markedly diminished unless pulmonary edema is present. The carbon dioxide tension of the blood is normal or decreased in heart failure. This is in contrast to the increase in CO_2 tension in emphysema. If the CO_2 content of the blood alone is studied, the respiratory acidosis of emphysema may be confused with the hypochloremic metabolic alkalosis which follows mercurial diuretics. There are occasional cases of concomitant pulmonary emphysema and left ventricular failure which are difficult to evaluate even when all pulmonary function studies are available.

The differentiation of polycythemia vera from polycythemia secondary to pulmonary disease is occasionally a problem. The evaluation of the roentgenogram of the lungs and simple pulmonary function tests usually permits one to make this differentiation without difficulty. The presence or absence of splenomegaly is helpful. Recent studies indicate that in secondary polycythemia the oxygen saturation of the hemoglobin of the arterial blood is decreased, whereas in polycythemia vera the saturation is normal (33).

TREATMENT

The recognition and adequate definition of pulmonary failure is important in the management of patients with pulmonary disease. While usually it is not possible to alter the basic pathology it is often possible to make the patient more comfortable and render his life more tolerable. The management of the patient in this regard differs little from the management of the patient with congestive heart failure.

The patient with pulmonary emphysema tends to be neglected, particularly in public clinics. This neglect is partly because of the apparent hopelessness of the disease and partly because of lack of knowledge of the physiologic mechanisms. This is unfortunate, because an interested and sympathetic physician can perform a great service for these patients.

The symptom of dyspnea causes real terror in many patients. It also appears that associated anxiety with consequent hyperventilation greatly exacerbates the dyspnea in certain patients. There is a wide variation in the subjective symptoms in pa-

tients with identical physiologic findings. Apparently, this difference is partly related to basic differences in personality and to differing psychologic reactions to the disease.

The comfort and support offered by a sympathetic physician may help a great deal in making the disease more tolerable. Moreover, the knowledge that help is available during an exacerbation of the disease is important to the patient. Another important aspect of the disease is the limitation of activity imposed by progressive loss of pulmonary function, which usually means that the patient has to adjust his work to meet his physical ability. As the disease progresses, he may be forced to give up his work and become dependent on others. All these changes lead to intense psychologic problems which the physician can often anticipate and help solve.

The physician can also contribute to the welfare of the patient by helping him avoid a futile search for a magic remedy or a better climate. By understanding the nature of his disease, the patient will know what is possible and what is impossible. In regard to climate, a permanent change of home seems inadvisable for most patients. The patient should continue his work as long as possible, but when this is no longer feasible, the web of relations, friends and associations in his home are of increased importance. Moreover, a move often requires a change in physicians, which is usually unwise. Today, with relative perfection in heating and air conditioning, the environment of the home differs little in various sections of the country.

Because of the tremendous importance of psychologic factors in these patients, it is difficult to evaluate certain types of therapy. Ritualistic forms of therapy such as chest exercise or intermittent positive pressure breathing are helpful to certain patients. Dramatic forms of therapy such as the use of pneumoperitoneum or radioactive iodine to suppress thyroid function seem to lead to improvement in others. The separation of the psychologic effects of this type of therapy from the physiologic effects seems an almost impossible task.

Recognition of pulmonary failure is also important in the consideration of patients for surgery. The function of the lungs often determines whether surgery is feasible in bronchiectasis, pulmonary tuberculosis and bronchogenic carcinoma. It is also important in estimating the volume of lung which may be removed safely.

Treatment of Infection

Chronic bronchitis is almost invariably associated with pulmonary emphysema. An exacerbation of this bronchitis usually occurs with an upper respiratory infection and frequently leads to a marked accentuation of dyspnea. At times, severe hypoxia and increase in CO_2 tension in the arterial blood may occur which may be associated with symptoms of right heart failure.

For some curious reason, the systemic manifestations of acute infection are often absent. The patient may have no fever or leukocytosis. If he is acutely ill, he may be unable to cough properly and hence purulent sputum may not be observed. This may be true even if pneumonia is present. For this reason, every patient with emphysema who has an acute exacerbation of dyspnea, evidence of severe hypoxia or right heart failure should be treated promptly and effectively for infection. The use of penicillin under these circumstances may be lifesaving and is probably the most important single measure. In this sense, its use is comparable to the use of digitalis in acute left ventricular failure.

Penicillin appears to be the antibiotic of choice in the management of acute bronchial infection. It can be administered by aerosol, but I prefer to administer it intramuscularly. Either crystalline penicillin or procaine penicillin may be used. Large doses appear to be more effective. Therapy should be continued until maximum improvement occurs, which may require 2-3 weeks. If the bacteria become resistant to penicillin, one of the broad-spectrum antibiotics may be used. Culture of the sputum and tests for sensitivity of the predominant organisms may be helpful under these circumstances.

The question of prolonged or prophylactic use of antibiotics is frequently raised. In general, this use appears to be unwise because of the danger of development of resistant bacteria and possible invasion by fungi. It appears best to treat the acute episodes of bronchitis and not use antibiotics during remissions.

Bronchodilators

Since the chief problem in pulmonary emphysema is interference with expiratory airflow, it is logical to use those agents which are known to produce bronchodilatation. It has been clearly shown experimentally that bronchodilators such as epinephrine improve pulmonary function. Clinically, the effect

is rather variable, but it is usually striking in those patients in whom pulmonary emphysema complicates bronchial asthma. In those patients with emphysema in whom there is no history of bronchial asthma and where no rales are present, the effect may be relatively slight. Nevertheless, this form of therapy is worthy of trial in all patients.

The use of Isuprel® hydrochloride (1:200) or epinephrine (1:100) by nebulizer appears to be most effective (6). A nebulizer which gives droplets of the proper size should be chosen. The technic is of great importance if effective results are to be obtained (31). Many patients use the nebulizer in an ineffective manner. The method of breathing is important. The patient should exhale maximally and then inhale slowly until the point of maximum inspiration is reached. At the end of inspiration he should hold his breath a few seconds. The patient then rests and repeats the procedure until the total dose has been utilized (½ cc.). Nebulization should be started before and continued through the maximum inspiration. Some people have great difficulty in using the hand bulb because of the necessary co-ordination of movement. In this case, an oxygen tank or air pump can be used as a source of gas pressure to generate the aerosol. A Y-tube can be attached to conserve the solution. The finger is placed over the open end of the Y-tube before inspiration.

Some physicians feel that the aerosol is more effective if administered with the intermittent positive pressure apparatus of Bennett. There is considerable difference of opinion on this point. However, it would be most reasonable to use a method which is suited to the individual patient and which will allow the aerosol to reach the smaller air passages in effective concentration.

Oral use of preparations containing ephedrine and aminophylline may be useful in certain patients.

Use of Oxygen

The use of oxygen in patients with severe pulmonary emphysema requires considerable thought and care. As mentioned earlier, the CO_2 stimulus to ventilation is relatively ineffective in patients with severe emphysema and hypercapnia. Hypoxia stimulates ventilation through chemoreceptors in the carotid and aortic bodies. Hence, in the hypoxic patient, administration of oxygen commonly leads to a decline in the level of

ventilation, an increase in CO_2 tension and a fall in blood pH. This in turn may lead to confusion, somnolence or coma. Fine tremors of the facial muscles and coarse twitching movements of the arms may be seen. Further depression of respiration may occur and death ensue (40).

The danger of CO_2 retention and respiratory acidosis should not completely obviate the use of oxygen therapy in patients with emphysema. Often in emphysema with a severe bronchitis the level of oxygen saturation may drop below 50%. The patient may die of hypoxia if oxygen is not administered. Oxygen is best administered by nasal catheter at a slow rate of flow, 1-3 liters per minute (6). The patient is carefully observed to determine whether his mental state is improving or becoming more depressed. The principle to be followed is one of trial and observation.

Patients with terminal pulmonary failure present a difficult problem. They have hypoxia, marked increase in CO_2 tension and decrease in blood pH. They do not tolerate oxygen, are usually stuporous or comatose and have no cough. Hence, secretions accumulate in the trachea and bronchi and further increase obstruction. Sieker and Hickam (36) have suggested a program for such patients. The patient should be bronchoscoped to remove excess mucous from the airway. The trachea is then intubated to allow suctioning of the tracheobronchial tree and to maintain a patent airway. An automatic respirator, either Drinker type, an intermittent positive pressure valve (Bennett) or a positive-negative automatic resuscitator (Seeler), is used to maintain adequate ventilation. An increased concentration of oxygen is used to correct anoxia. Bronchodilators, steroids and antibiotics are also administered.

Use of Sedatives

In acute episodes of pulmonary failure, sedatives are extremely dangerous. This is particularly true of morphine, but Demerol® and barbiturates also may be hazardous. There appears to be a synergistic effect between the increase in arterial CO_2 tension and the sedative which leads to a profound decrease in ventilation (41). The combination of morphine and oxygen is particularly lethal. For this reason, it is important to distinguish between acute left ventricular failure and pulmonary failure with cor pulmonale.

The temptation to use sedatives in patients with hypoxia and

CO_2 retention is great. These patients often are irrational and restless, making them difficult to manage. The only effective relief comes from improvement of ventilation.

Mild sedatives such as chloral hydrate can be used in patients with emphysema who do not have marked hypoxia or CO_2 retention.

Use of Adrenal Cortical Hormones

Use of the adrenal steroids in patients with pulmonary failure has been a controversial subject. Although cortisone and ACTH may give remarkable relief to patients with bronchial asthma who have become refractory to other forms of therapy (20), the use of these agents in pulmonary emphysema is much more controversial. They would not appear to play a part in therapy in most patients. In the instance of pulmonary emphysema complicating bronchial asthma the adrenal steroids may have some value (6). However, improvement usually disappears when the steroids are withdrawn and complications and side effects may be associated with long-term therapy.

The use of adrenal steroids in diffuse interstitial fibrosis of the lungs is also controversial. Obviously, the use of these agents should be avoided if the underlying disease is tuberculosis or fungous infection. The steroids may have some value in progressive pulmonary sarcoidosis with impairment of pulmonary function. The value of these agents in the Hamman-Rich syndrome is not entirely clear.

Management of Congestive Heart Failure

Right ventricular failure usually complicates pulmonary disease when hypoxia is severe. It is particularly prone to occur when severe pulmonary emphysema is complicated by acute bronchitis with consequent severe impairment of alveolar ventilation. Therapy should be aimed primarily at improving ventilation and relieving hypoxia. Antibiotic therapy is particularly important. Death usually results from hypoxia or respiratory acidosis rather than from congestive heart failure. Relief of the hypoxia will usually lead to disappearance of the signs of right ventricular failure.

The usual therapy for congestive heart failure is commonly used. While digitalis has been demonstrated to increase cardiac output in cor pulmonale (16) the clinical effects are usually

not striking. The most dramatic effects are observed in those occasional instances where left ventricular failure and pulmonary emphysema coexist.

A low-salt diet and mercurial diuretics may be used to combat edema. Some clinicians believe Diamox® has special merit in pulmonary emphysema. Because it is a carbonic anhydrase inhibitor, it leads to a loss of sodium and bicarbonate in the urine. The loss of bicarbonate in the urine leads to a decrease in blood bicarbonate and a decrease in blood pH. Associated with this decrease may be an increase in ventilation (24). Caution should be exercised in using Diamox® in acute respiratory acidosis as it may lead to a further decrease in blood pH.

Venesection

Many patients with pulmonary emphysema and hypoxia demonstrate no increase in the erythrocyte count or hemoglobin content of the blood. Occasionally, patients exhibit marked polycythemia which also may be seen in other types of pulmonary failure. The increase in hemoglobin content of the blood is beneficial in that more oxygen is transported to the tissues at a given level of cardiac output. The increase in hemoglobin content of the blood in people living at high altitudes may be marked and is considered to be an important compensatory response to hypoxia. The disadvantage of polycythemia is that it leads to an increase in the viscosity of the blood and hence may accentuate the existing pulmonary hypertension.

Whether venesection should be done in secondary polycythemia associated with pulmonary disease seems to be a matter of personal preference. I feel that it is not indicated unless the hematocrit reading rises to very high levels.

Other Therapeutic Measures

Irritants to the mucosa of the bronchi should be avoided in patients with emphysema. Any dusty environment may accentuate symptoms. Recently, the ill effects of smoking have been emphasized because a careful study indicates that smoking one cigarette increases resistance to airflow in patients with emphysema (15). Therefore, it would be wise for these patients to cease smoking.

Weight reduction is essential in those patients with the syndrome of marked obesity and pulmonary insufficiency. Not only is additional effort required to move about, but also obesity interferes with the normal mechanics of breathing. Most patients with serious pulmonary insufficiency lose weight spontaneously as a result of anorexia.

Breathing exercises are considered important by some in the treatment of emphysema (6). Others can demonstrate little effect of such exercises. Certainly excessive effort in forcing expiration is futile and should be avoided. Pneumoperitoneum, as a treatment of emphysema, seems to be falling into disfavor. Surgical treatment of pulmonary emphysema is occasionally used, but at present it is usually restricted to patients with large bullae and atelectasis of the adjacent lung (18).

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